What is claimed is:

1. An isolated nucleic acid molecule encoding a SEL-12.

2. An isolated nucleic acid molecule encoding a mutated SEL-12.

3. An isolated nucleic acid molecule of claim 2, wherein the mutated SEL-12 contains at least one of the following: leucine at position 115, arginine at position 132, glutamic acid at position 215, valine at position 229, valine at position 254, valine at position 255, valine at position 371, tyrosine at position 387, isoleucine at position 104 or valine at position 204.

4. An isolated nucleic acid molecule of claim 2, wherein the mutated SEL-12 contains one or more alterations.

5. An isolated nucleic acid molecule encoding a *Caenorhabditis elegans* protein that is homologous to SEL-12.

6. An isolated DNA molecule of claim 2 or 3, wherein the mutation is generated by in vitro mutagenesis.

SUB A1

7. An isolated DNA molecule of any of claim 1 to 6.

8. An isolated cDNA molecule of claim 7.

9. An isolated genomic DNA molecule of claim 7.

SUB A2

10. An isolated RNA molecule of any of claim 1 to 6.

11. An isolated nucleic acid molecule of claim 1, wherein the SEL-12 has substantially the same amino acid sequence as the amino acid sequence shown in Figure 1A.

SUB A3

12. A nucleic acid molecule of at least 15 nucleotides capable of specifically hybridizing with a unique sequence within

SUB A3

the sequence of a nucleic acid molecule of claim 1.

13. A DNA molecule of claim 12.

14. An RNA molecule of claim 12.

15. A vector which comprises the isolated nucleic acid molecule of claim 1.

16. An isolated nucleic acid molecule of claim 7, 8 or 9 operatively linked to a promoter of RNA transcription.

SUB A4

17. The vector of claim 15 or 16, wherein the vector is a plasmid.

18. The plasmid of claim 17 designated pMX8 (ATCC Accession No. 97278).

19. The plasmid of claim 17 designated p1-1E (ATCC Accession No. 97279).

20. A host vector system for the production of a SEL-12 protein which comprises the vector of claim 15 and a suitable host.

21. A host vector system of claim 20, wherein the suitable host is a bacterial cell, insect cell, plant or mammalian cell.

22. A purified SEL-12 protein or a fragment thereof.

23. A purified mutated SEL-12 protein or a fragment thereof.

24. A method for production of an antibody comprising:

a) administering an amount of the purified protein or fragment of SEL-12 or mutated SEL-12 to a suitable animal effective to produce an antibody against SEL-12 or mutated SEL-12 protein in the animal; and

b) recovering the produced antibody so produced from the

animal.

25. A method for production of an antibody capable of binding to wild-type or mutant S182 or E5-1/STM2, wherein the antibody is produced by in vitro immunization.

26. A method for production of an antibody capable of binding to wild-type or mutant S182 or E5-1/STM2, wherein the antibody is produced by screening a differential phage display library.

27. A method for production of an antibody capable of binding to wild-type or mutant S182 or E5-1/STM2 comprising:
a) determining conserved regions revealed by alignment of the SEL-12, S182 and E5-1/STM2 protein sequences;
b) synthesizing peptides corresponding to the revealed conserved regions;
c) administering an amount of the synthesized peptides to a suitable animal effective to produce an antibody against the peptides in the animal; and
b) recovering the produced antibody so produced from the animal.

28. An antibody produced by the method of any of claim 24 to 27.

29. A monoclonal antibody of claim 28.

30. A transgenic animal comprising a DNA molecule of any of claims 7 to 9.

31. The transgenic animal of claim 30 wherein the animal is a *Caenorhabditis elegans*.

32. A transgenic *Caenorhabditis elegans* animal comprising wild-type or mutant human S182 gene.

33. A transgenic *Caenorhabditis elegans* animal comprising wild-type or mutant human STM2/E5-1 gene.

34. A transgenic *Caenorhabditis elegans* animal comprising wild-type or mutant human presenilin gene.

35. A transgenic *Caenorhabditis elegans* animal of any of claim 30-34, wherein the wild-type or mutant human S182, or wild-type or mutant STM2/E5-1 gene, or mutant human presenilin gene is under the control of *sel-12* or *lin-12* regulatory sequence.

36. A transgenic *Caenorhabditis elegans* animal of claim 30-34, wherein the wild-type or mutant human S182, or wild-type or mutant STM2/E5-1 gene, or mutant human presenilin gene is under the control of a regulatory sequence other than the *sel-12* or *lin-12* regulatory sequence.

37. A transgenic *Caenorhabditis elegans* animal of claim 30-36 having an egg-laying constitutive (Egl^c) phenotype.

38. A transgenic *Caenorhabditis elegans* animal of claim 30-36 having a phenotype other than egg-laying constitutive (Egl^c).

39. A transgenic *Caenorhabditis elegans* animal having a *sel-12* allele that reduces, eliminates or elevates *sel-12* activity.

40. A transgenic *Caenorhabditis elegans* animal having a *sel-12* transgene carrying a mutation that is equivalent to a mutation that causes Alzheimer's disease [*sel-12(Alz)*].

41. A method for identifying a compound which is capable of ameliorating Alzheimer disease comprising administering effective amount of the compound to the transgenic animal of any of claim 30-40, the alteration of the conditions of the transgenic animal indicating the compound is capable of ameliorating Alzheimer's disease.

42. A method of claim 41, wherein at least one signalling pathway is altered.

43. A method of claim 42, wherein the signalling pathway is a neuronal signalling pathway.

44. A method of claim 43, wherein the signalling pathway is the serotonergic signalling pathway.

45. A previously unknown compound identified by the method of any of claim 41-44.

46. A pharmaceutical composition comprising an effective amount of the compound identified by the method of claim of any of 41-44 and a pharmaceutically acceptable carrier.

47. A method for determining whether a compound is capable of ameliorating Alzheimer's disease comprising:

a) treating *Caenorhabditis elegans* mutants having reduced, increased or altered *sel-12* activity with the compound; and

b) determining whether the compound suppresses, enhances or has no effect on the phenotype of the mutant, the suppression or enhancement of the phenotype indicating that the compound is capable of ameliorating Alzheimer's disease.

48. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is *sel-12(ar171)* (ATCC Accession No. 97292).

49. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is *sel-12(ar131)* (ATCC Accession No. 97293).

50. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is a *sel-12* allele that reduces or eliminates *sel-12* activity.

51. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is a *sel-12* allele that elevates or alters *sel-12* activity.

52. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is a *sel-12* transgenic animal carrying a mutation in *sel-12* that is equivalent to a mutation that causes Alzheimer's disease [*sel-12(Alz)*].

53. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is a *sel-12* transgenic animal carrying a mutation in *sel-12*, and results in an Egl^c phenotype.

54. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is a *sel-12* transgenic animal carrying a mutation in *sel-12* that is equivalent to a mutation that causes Alzheimer's disease, and results in a phenotype other than Egl^c phenotype.

55. A method of claim 47, wherein the *Caenorhabditis elegans* mutant to be treated is a transgenic animal from any of claim 30-40.

56. A previously unknown compound determined by the method of any of claim 47-55 to be capable of ameliorating Alzheimer's disease.

57. A pharmaceutical composition comprising an effective amount of the compound determined by the method of claim 47-55 to be capable of ameliorating Alzheimer's disease and a pharmaceutically acceptable carrier.

58. A method for identifying a suppressor of the multivulva phenotype of *lin-12* gain-of-function mutation comprising:

a) mutagenizing *lin-12 Caenorhabditis elegans* worms with an effective amount of an appropriate mutagen;

b) screening for revertants in the F1, F2 and F3 generations; and

c) isolating the screened revertant, thereby identifying a suppressor of the multivulva phenotype of *lin-12* gain-of-function mutation.

59. A suppressor identified by method of claim 58.

60. An animal having a suppressor of claim 59, designated *sel-12(ar131)* (ATCC Accession No. 97293).

61. An animal having a suppressor of claim 59, designated *sel-12(ar133)*.

62. A method for identifying a mutant *sel-12* gene which reduces *sel-12* function comprising:

a) mutagenizing *Caenorhabditis elegans* worms with an effective amount of an appropriate mutagen;

b) performing complementation screening of the mutagenized worms to determine if a descendant of a mutagenized worm bears a mutation that fails to complement a suppressor of claim 59 for the Egl defect; and

c) isolating the individual worm and determining the phenotype of worms carrying the new allele in its homozygous form and *in trans* to a deficiency, thereby identifying a mutant *sel-12* gene which reduces *sel-12* function.

63. A method for identifying a mutant *sel-12* gene which reduces or elevates *sel-12* function comprising:

a) mutagenizing *Caenorhabditis elegans* worms with an effective amount of an appropriate mutagen;

b) identifying suppressors or enhancers of *daf-1* single mutants, or *daf-1; sel-12* double mutants, or mutations in other genes that interact with *sel-12;*

c) isolating the individual worm and determining the phenotype of worms carrying the new allele in its homozygous form and *in trans* to a deficiency, thereby identifying a mutant *sel-12* gene which reduces *sel-12* function.

64. A method of claim 63, further comprising performing DNA sequence analysis of the identified mutant *sel-12* gene to determine the molecular lesion responsible for the

mutation.

65. A mutant *sel-12* gene identified by the method of any of claim 62-64.

66. An animal having a mutant *sel-12* gene of claim 62, designated *sel-12 (ar171)* (ATCC Accession No. 97292).

67. A method for producing extragenic suppressors or enhancers of a *sel-12* allele comprising:
a) mutagenizing *sel-12* mutant hermaphrodites with an effective amount of a mutagen;
b) screening for revertants in the F1, F2 and F3 generations; and
c) isolating the screened revertant, thereby producing extragenic suppressors or enhancers of a *sel-12* allele.

68. A method for producing extragenic suppressors of a *sel-12* allele comprising:
a) mutagenizing *sel-12(ar171) or sel-12(ar131)* mutant hermaphrodites with an effective amount of a mutagen;
b) screening for revertants in the F1, F2 and F3 generations; and
c) isolating the screened revertant, thereby producing extragenic suppressors or enhancers of a *sel-12* allele.

69. A method for producing extragenic suppressors or enhancers of a *sel-12* allele comprising:
a) mutagenizing *daf-1(m213); sel-12(ar171)* mutant hermaphrodites with an effective amount of a mutagen;
b) screening for revertants in the F1, F2 and F3 generations; and
c) isolating the screened revertant, thereby producing extragenic suppressors or enhancers of a *sel-12* allele.

70. A method for producing extragenic suppressors or enhancers

of a *sel-12(Alz)* mutant comprising:

a) mutagenizing *sel-12 (Alz)* hermaphrodites with an effective amount of a mutagen;

b) screening for revertants in the F1, F2 and F3 generations; and

c) isolating the screened revertant, thereby producing extragenic suppressors or enhancers of a *sel-12(Alz)* mutant.

71. A suppressor or enhancers produced by the method of any of claim 67-70.

72. A suppressor of presenilin, designated *spr-1, spr-2, spr-3 or spr-4*.

73. The human homolog of *spr-1, spr-2, spr-3 or spr-4*.

74. A human homolog of a gene defined by extragenic suppressor or enhancer of a *sel-12* mutant.

75. A Drosophila homolog of a gene defined by extragenic suppressors of a *sel-12* mutant.

76. A mouse homolog of a gene defined by extragenic suppressor of a *sel-12* mutant.

77. The homolog of any of claim 73-76, wherein the *sel-12* mutant is *sel-12(ar171)* (ATCC Accession No. 97292).

78. The homolog of any of claim 73-76, wherein the *sel-12* mutant is *sel-12(Alz)* transgene.

79. The homolog of any of claim 73-76, wherein the *sel-12* mutant is *sel-12(ar131)* (ATCC Accession No. 97293)

80. The homolog of any of claim 73-76, wherein the *sel-12* mutant is any other *sel-12* allele.

81. A method for identifying a suppressor gene comprising

performing DNA sequence analysis of the suppressor of claim 68 to identify the suppressor gene.

82. The suppressor gene identified by method of claim 81.

83. A human suppressor gene of claim 82.

84. A Drosophila suppressor gene of claim 82.

85. A mouse suppressor gene of claim 82.

86. The method of any of claim 59, 60, 61, 65, 66 or 67, wherein the mutagen is ethyl methanesulfonate.